TB Suspect Case Presentation and Discussion

David E. Griffith, M.D.
Assistant Medical Director
Heartland National TB Center

Diagnosis of Tuberculosis

• Clinical suspicion is the single most important factor in the timely diagnosis of tuberculosis.
• The greatest risk for nosocomial transmission of tuberculosis is exposure to an undiagnosed case of TB.
• There is no diagnostic substitute for thinking about the diagnosis.

Good Outcomes Depend on Complete Evaluation and a Correct Diagnosis

• Medical Evaluation
  – Signs and symptoms
  – History of risk factors and/or exposures
  – Physical exam
• Chest X-ray
• Bacteriology
  – Cultures of suspected site
  – Susceptibility testing of positive isolate
  – Rapid diagnostic tests (HPLC, NAA)
Postprimary (Reactivation) Disease

• “Parenchymal opacities situated in the apical and posterior segments of the upper lobes and the superior segment of the lower lobes, often associated with cavitation, are the characteristic radiographic manifestations of postprimary TB.”

Progressive Primary TB: Radiographic Findings

• Parenchymal disease: areas of greatest ventilation-lower and middle lobes
• Lymphadenopathy
• Pleural effusion
• Miliary tuberculosis
• Obstructive atelectasis due to lymphadenopathy
• Normal chest radiograph

TB and AIDS: Radiographic Appearance

• The radiographic manifestations of HIV-associated pulmonary TB are dependent on the level of immuno-suppression.
  – Relatively intact cellular immune function (CD4 > 200): radiographic findings similar to non-HIV infected individuals (upper lobe, cavitary disease)
  – Severe immunosuppression (CD4 < 200): findings c/w primary disease or normal chest radiographs or dissemination with miliary pattern or extrapulmonary disease
Atypical Presentation of TB

- HIV infection, chronic renal disease, diabetes, immunosuppression may alter presentation
  - CXR may be atypical; lower lobe infiltrate, adenopathy or completely normal
  - Negative TST or QFT Gold
  - Negative smear in up to 50%
  - Atypical clinical presentation

Reasons a Diagnosis of TB is Missed or Delayed

- Patient is diagnosed as a community acquired pneumonia and responds to a fluoroquinolone
- Atypical clinical and radiographic picture
- Extrapulmonary disease
- Clinician does not consider TB a diagnosis

Delayed TB Diagnosis

- Patient from Mexico in his mid 30’s, in the U.S. more than a year, presented to local ED with cough, fever
- Patient treated with oral fluoroquinolone with mild, transient improvement, but symptoms relapsed
- Represented to ED and given FQ again, little symptomatic change
- After 4 months, seen in different ED, sputum sent for AFB which was 4+ AFB positive
Delayed TB Diagnosis

- Patient with multiple contacts: family, co-workers, healthcare workers and multiple skin test conversions
- Started on RIPE, *M. tuberculosis* isolate susceptible to first line medications
- Successfully treated with 9 months standard medication

Delay in Diagnosis of TB With Empiric Antibiotic Use

- Prospective study to assess delay in diagnosis
  - 85/158 TB patients received antibiotics for non-TB dx before TB dx
    - 30 patients received more than one course
    - 52 courses FQN to 45 patients (38%)
    - 33 courses macrolides to 29 patients (24%)
    - 11 courses amoxicillin
    - 11 courses cephalosporins
    - 10 courses trimethoprim-sulfamethoxazole
    - 2 courses of clindamycin, 1 of vancomycin
    - 17 courses unknown

Delay in Diagnosis of TB With Empiric Antibiotic Use

- Median delay 39 days compared to 15 controls who did not receive antibiotics
- Delay similar with all antibiotic classes
- 41/54 (79%) patients who did not get CXR at first visit received antibiotics
- 41/105 (42%) with CXR at 1st visit received antibiotics
  - 31/54 (57%) dx with CAP received CXR
- More widespread use of CXR may help

Int J Tuberc Lung Dis 2005;9:392-397

Impuerial treatment of community-acquired pneumonia and the development of fluoroquinolone-resistant TB.

Long et al, Clin Infect Dis 2008; 48: 1354-60

- 74/428 patients with TB had received \( \geq 1 \) fluoroquinolone (FQ) prescription within 6 months of TB diagnosis
- 3/148 M. tuberculosis isolates FQ resistant: all patients had received multiple FQ prescriptions
- Single FQ prescriptions not associated with FQ resistance, but multiple FQ prescriptions were associate with FQ resistance.

Case 1: OE

- 29 yo man from Mexico, in the U.S. 4 years, frequent travel to Florida, Mexico
- One year of symptoms including cough, fever, malaise, weight loss
- Abnormal CXR with cavity treated as community acquired pneumonia on multiple occasions
- Referred to DSHS for enlarging cavity
Case 1: OE

- 31 contacts tested by DSHS
- Multiple children (family and non-family) cared for in the patient’s home
- 21 (+) PPD results
- 6 active cases, all children (ages 1 yr, mos to 10 yrs, 8 mos)

Case 2: IM

- 2 yrs 3 mos old female
- Contact to OE
- Asymptomatic
Case 4: VM

- 2 yrs 3 mos male
- Contact to OE
- Asymptomatic
Delayed TB Diagnosis

- 25 yr old male with 9 month history of cough and weight loss
- ER visit 6 months earlier for "bronchitis"
- Incarcerated along border x 2 yrs
- Large # family contacts and small children
- Worked as a caterer
- Picked up from mall by EMS due to severe coughing spell
Delayed Diagnosis of TB

- 32 yo female immigrant from high incident area (FSU), homelessness, incarceration, IVDU, exposure to TB
- prolonged cough, sputum, fever, weight loss, night sweats
- Positive tuberculin skin test (TST) (no therapy)
- Positive QuantiFeron TB Gold Test
- CXR with upper lobe cavitary infiltrates
Delayed TB Diagnosis

- Abnormal chest radiograph, AFB smears and cultures initially negative
- Dental abscess, treated with PCN as aspiration pneumonia
- Several months later, presented with hemoptysis, weight loss
- Sputum AFB smear and culture (+) for INH resistant TB

Tuberculosis in the Foreign-born

Risk for drug resistant TB

Entering the U.S. with Active TB

- Enter the U.S. as a tourist, for business, as a student or as a temporary worker, etc…
- Enter the U.S. illegally
- A classification on medications
- B1 classification with false negative smears
- B2 classification with false negative CXR
- "Asymptomatic" children, (immuno-compromised adults) with primary TB
Delayed TB Diagnosis

- 32 yo man recently entered the U.S. from Ethiopia
- History of 2 episodes of previous TB therapy
- Initial sputum AFB smear negative, QFT TB-gold (+)
- Treated initially for community acquired pneumonia

Global Epidemiology of Multidrug Resistant (MDR) TB

- MDR TB: Resistant to INH and Rifampin
- Estimated global prevalence of multidrug (MDR) resistant TB
  - Estimated 500,000 cases
  - Newly diagnosed cases: 2.3%
  - Previously treated cases: 16.4%
Definitions of Drug Resistant Tuberculosis

- MDR TB is the precursor of XDR TB
- XDR TB: MDR TB
  - PLUS
  - Resistance to any fluoroquinolone
  - Resistance to at least one of the following injectables:
    - Amikacin, Kanamycin, Capreomycin

Drug Resistant Tuberculosis Creation of XDR TB

- The development of XDR TB results from TB control and treatment practices in most of the world that would not be acceptable in the United States
- Case identification and treatment response are based on AFB smears without confirmatory cultures or susceptibility testing.
- Retreatment for treatment failure not based on in vitro susceptibility studies, rather, on fixed retreatment regimens.
Delayed TB Diagnosis

- Patient did not improve with antibacterial therapy
- Repeat sputum AFB smear and culture positive
- *M. tuberculosis* isolate susceptible to all first line antituberculosis drugs (whew!)
- Patient successfully treated

Entering the U.S. with Active TB

- Mr. RF, 71 yo man from China
- Entered the U.S. as tourist to visit his children in Houston
- Treated multiple times in China for tuberculosis without success (unknown at time of entry to U.S.)
- Presented for medical evaluation because of cough and shortness of breath
Entering the U.S. with Active TB

- RF’s sputum 4+ AFB smear pos, culture pos for MTB resistant to: INH, Rif, Rbt, EMB, PZA, STM, AMK, fluoroquinolones
- Treated with Eth, Cap, Cyc, PAS, linezolid
- Within 3 mos, sputum converted to AFB smear and culture negative
- Hospitalized 4 mos, returned to Houston

Difficult Tuberculosis Diagnosis

Extra-pulmonary TB
**Fever in 7th month of Pregnancy**

6 month history of cervical adenopathy
6 week history of fever, weight loss and abdominal pain
Tuberculin skin test negative
No response to multiple antibiotics
Pleural effusion and infiltrate on CXR

**Delayed TB Diagnosis**

Pulmonary consult for thoracentesis:
Cervical node biopsy: AFB+, granuloma
Disseminated disease
- nodes, lung, liver, ascites, multiple abdominal masses, **placenta**, ovaries, bowel
Clinical deterioration, hypotension, emergent C section
Missed Diagnosis

Pulmonologist consulted for thoracentesis obtained a **history of risk factors** for TB

Born in Mexico
Prior +TST at US entry at age 15
Treated with INH x 6 mo
Exposure to uncle in Mexico who died with TB 2 years ago

*TST usually negative with extensive disease*

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Delayed TB Diagnosis

M Tb resistant to INH grew from sputum and nodes
Infant also treated for tuberculosis as placenta was positive for AFB
Mother and child recovered from TB

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Guidelines for Evaluation of Pulmonary TB in Adults

- Any cough ≥ 2-3 wks plus at least **one** additional symptom: fever, night sweats, weight loss or hemoptysis
- Any high risk for TB: unexplained illness including respiratory symptoms ≥ 2-3 wks
- **CXR:** if suggestive of TB collect 3 sputum specimens for AFB and culture

Controlling TB in U.S. MMWR: Nov 2005
Guidelines for Evaluation of Pulmonary TB in Adults

- Any HIV infected with unexplained cough and fever
- Any at high risk for TB with dx CAP & not improved >7 days
- Any at high risk for TB with incidental findings on CXR of TB even minimal/no sx

- CXR and collect 3 sputum for AFB smear and culture
- CXR and 3 sputum for AFB smear and culture
- Review prior CXR if available, 3 sputum for AFB smear and culture

Controlling TB in U.S. MMWR: Nov 2005